REMARKS

In response to the Office Action mailed January 11, 2008, Applicant amends claim 1 and submits the following remarks. Claims 1-4, 6-17, 19-31, 49-54, and 56-59 are pending, with claim 16 withdrawn from consideration.

The Examiner rejected claims 1, 2, 8, 9, 15-17, 19-23, 25, 26, 28-31, 49-54, and 56-59 under 35 U.S.C. § 103(a) as being unpatentable over Jacobsen et al., US 6,530,943 ("Jacobsen") and Greene et al., US 2002/0177855 ("Greene"), in view of Smith et al., US 5,888,930 ("Smith").

Claims 1, 2, 8, 9, 15-17, 19-23, 25, 26, 28-31, 49-54 and 56-59 cover compositions that include particle chains having at least two connected particles and a link that connects the at least two connected particles. At least one of the at least two connected particles has an interior region with pores having a mean size and a surface region with pores having a mean size, where the mean size of the pores of the interior region is greater than the mean size of the pores of the surface region.

Without conceding that such would be the case, even if one skilled in the art would have somehow wanted to try to combine the teachings of these references, the result would not have been the subject matter covered by claims 1, 2, 8, 9, 15-17, 19-23, 25, 26, 28-31, 49-54 and 56-59 for at least the following reasons.

The Examiner asserted that Jacobson discloses a particle chain. Without conceding that such is true, even if Jacobsen could be construed as disclosing a particle chain, Jacobson does not disclose how to make his particle chain. Instead, Jacobson only discloses the various shapes of the particle chains and their components, which are the particles or the beads. (See, e.g., Jacobsen, FIGS. 4-8, col. 9 line 22 to col. 10 line 28, FIGS. 9-11, and col. 10 line 35 to col. 11 line 8.) Further, the particles in Jacobson's particle chain does not include the features of the particles covered by claims 1, 2, 8, 9, 15-17, 19-23, 25, 26, 28-31, 49-54 and 56-59, i.e., at least one of the at least two connected particles has an interior region with pores having a mean size and a surface region with pores having a mean size, where the mean size of the pores of the interior region is greater than the mean size of the pores of the surface region.

There is no teaching regarding how the particle chain disclosed in Jacobsen could be modified to include the particles disclosed in Smith. Smith discloses particles that include continuously-gradated asymmetric microporous structures. In this regard, Smith reads:

> The beads of the present invention are made of film-forming polymers, they have a generally spherical shape with diameters ranging from about 5 microns to about 5 mm, and they have a unique, continuously-gradated asymmetric microporous structure, with small pores near the surface and progressively larger pores toward the interior core. They are typically loaded with active ingredient following preparation of the beads, and the active ingredient is released at a slow and substantially constant rate over an extended period of time. (Smith, col. 2, lines 47-56.)

To make his particle with such features, Smith further teaches:

> The key to achieving the characteristic continuously-gradated asymmetric pore structure of the beads of the present invention is keeping the rate of solvent exchange with the liquid of the precipitation bath slow following a rapid initial precipitation that forms the "skin" layer. (Id., col. 3, lines 6-10.)
>
> In order to achieve the continuously-gradated pore structure of the beads of the present invention, the polymer, its solvent, and the precipitation bath must all be specified. Examples of polymer/solvent bath combinations that result in asymmetric microporous beads of the invention include: polysulfone/dimethylformamide/water, polyvinylidenefluoride/dimethylformamide/water-dimethylformamide; polyvinylchloride/dimethylformamide/water dimethylformamide; polyurethane/dimethylformamide/water; and cellulose acetate/dichloromethane-dimethylformamide/water.
>
> The beads of the present invention are prepared by first dissolving the polymer in a solvent or solvent mixture, then spraying droplets of the solution thus formed into a stirred precipitation bath containing a liquid, typically water, that is miscible with the solvent, allowing the precipitated beads to remain in the bath until substantially all of the solvent has been removed or exchanged, and then collecting the beads and drying them, if desired. (Id., col. 3, lines 49-67.)

Accordingly, after reading Smith, one skilled in the art would understand that to make Smith's particles with the desired features, one must carefully select the proper materials that are suggested by Smith and strictly follow the processes Smith teaches. Thus, one skilled in the art would not have even wanted to try to modify Smith's process to produce particle chains. Even if such a person had tried to do so, that person would not have known how to make Smith's particles into a Jacobsen's particle chain, since neither Jacobsen nor Smith, teaches methods of making such chains.

In response to Applicant's arguments, the Examiner states:

> Applicant argues on pages 9-11 of the response that Jacobsen does not teach how to make his particle chain, and that in order for the prior art to render the subject matter covered by a claim obvious, the prior art must enable one skilled in the art how to make and use the subject matter.

This is found non-persuasive because prior art is presumed to be operable/enabling per MPEP 2121. When the reference replied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability. *In re Sasse*, 629 F.2d 675, 207 USPQ 107 (CCPA 1980). In addition, under 35 U.S.C. 282 a patent shall be presumed valid (i.e. and thus is presumed to meet the enablement requirement). (Office Action, page 7.)

It is well established, however, that, for the prior art to render the subject matter covered by a claim obvious, the prior art must enable one skilled in the art to make and use the subject matter being claimed. (See, e.g., Beckman Instruments, Inc. v. LKB Produkter AB, 892 F.2d 1547, 1551 (Fed. Cir. 1989)). Thus, even if Jacobsen did providing an enabling disclosure for how to make his particle chains, one skilled in the art would not know how to a chain of the type disclosed by Jacobsen with the particles disclosed by Smith at least because, as explained above, Smith's particles can be made only with the specific methods Smith taught, and Jacobsen's particles in the particle chains do not have the features of Smith's particles and are not made using Smith's methods. Therefore, even if one skilled in the art would have found it obvious to try to combine Jacobsen and Smith, that person would not have been able to make Smith's particles in Jacobsen's particle chains.

Greene's methods of making his embolization device are not even compatible with Smith's methods of making his beads. Greene's methods involve putting a polymer member in a tubular holder followed by coaxially skewering the polymer member with the filamentous carrier, or disposing a filamentous carrier in a mold followed by transferring polymer under pressure into the mold. (See, e.g., Greene, paragraphs [0021] through [0024].)

In contrast, Smith makes his particles by spraying droplets of a polymer solution into a precipitation bath and dry the droplets to form individual beads. (See, e.g., Smith, col. 3, lines 60-67 and col. 4, lines 50-53). As explained above, to make Smith's particles, one has to carefully select the materials Smith suggested and strictly follow the method Smith teaches. After reading Smith and Greene, one skilled in the art would understand that Greene's method would not be suitable for making Smith's particles. Thus, it would not have been obvious to one skilled in the art to try to combine the references in the manner suggested by the Examiner, and, even if it would have been obvious to try to do this, the references would not have enabled the

person to make the subject matter covered by claims 1, 2, 8, 9, 15-17, 19-23, 25, 26, 28-31, 49-54 and 56-59.

In response to Applicant's arguments, the Examiner states:

> This is found non-persuasive because, it is unclear why, for example, the polymeric particles of Smith could not at least be skewered in order to arrive at linked particles having the claimed pore size distribution. Furthermore, see MPEP 2145 (III) regarding arguing that prior art devices are not physically combinable. "The test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference ... Rather, the test is what the combined teachings of those references would have suggested to those of ordinary skill in the art." *In Re Keller*, 642 F. 2d 413, 425, 208 USPQ 871, 881 (CCPA 1981). See also *In re Sneed*, 710 F. 2d 1544, 1550, 218 USPQ 385, 389 (Fed. Cir. 1983) ("[I]t is not necessary that the inventions of the references be physically combinable to render obvious the invention under review."); and *In re Nievelt*, 482 F .2d 965, 179 USPQ 224, 226 (CCPA 1973) ("Combining the teachings of references does not involve an ability to combine their specific structures.")

However, it is well established that the reasonable expectation of success must both be found in the prior art, not in the applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991.) (MPEP §2143.) As explained above, after reading Greene and Smith, one skilled in the art would not have had a reasonable expectation of success in trying to make Smith's particles using Greene's methods that include coaxially skewering a polymer member with the filamentous carrier, or disposing a filamentous carrier in a mold followed by transferring polymer under pressure into the mold. Therefore, it would not have been obvious to one skilled in the art to combine Greene and Smith to provide the Greene's particle chain with Smith's particles.

None of Jacobsen, Greene, or Smith, alone or in combination discloses or renders obvious the subject matter covered by claims 1, 2, 8, 9, 15-17, 19-23, 25, 26, 28-31, 49-54 and 56-59. Accordingly, Applicants request reconsideration and withdrawal of the rejection of claims 1, 2, 8, 9, 15-17, 19-23, 25, 26, 28-31, 49-54 and 56-59 under 35 U.S.C. § 103(a) as being unpatentable over Jacobsen and Greene, in view of Smith.

The Examiner rejected claims 1-4, 6-15, 17, 19-26, 28-31, and 49-59 under 35 U.S.C. § 103(a) as being unpatentable over Jacobsen and Greene, in view of Smith, and in further view of Mazzocchi et al., US 6,605,102 ("Mazzocchi").

For the reasons noted above, the combination of Jacobsen, Greene and Smith does not render the subject matter covered by claims 1-4, 6-15, 17, 19-26, 28-31, 49-54 and 56-59 unpatentable under 35 U.S.C. § 103(a). Mazzocchi does not cure the deficiencies of these references, at least because Mazzocchi does not disclose or render obvious the compositions including the particle chains as covered by these claims, and certainly does not disclose or otherwise indicaate how to make such particle chains. None of Jacobsen, Greene, Smith or Mazzocchi, alone or in combination discloses or renders obvious the subject matter covered by claims 1, 2, 8, 9, 15-17, 19-23, 25, 26, 28-31, 49-54 and 56-59. Applicants therefore request reconsideration and withdrawal of this rejection.

The Examiner rejected claims 1-7, 15, 17, 19, 21, 22, 25-31, 49-54, and 56-59 under 35 U.S.C. § 103(a) as being unpatentable over Jacobsen in view of Mangin, WO 01/66016 ("Mangin").

Claims 1-7, 15, 17, 19, 21, 22, 25-31, 49-54 and 56-59 cover compositions that include particle chains having at least two connected particles and a link that connects the at least two connected particles. At least one of the at least two connected particles has an interior region with pores having a mean size and a surface region with pores having a mean size, where the mean size of the pores of the interior region is greater than the mean size of the pores of the surface region.

Neither Jacobsen nor Mangin, either alone or in combination, discloses or renders obvious such particle chains. Jacobsen discloses a particle chain, but, as explained above, he does not disclose how to make his particle chain. Mangin does not disclose or render obvious particles that are included in a particle chain. Instead, Mangin discloses an embolic particle that has voids present within the particle as well as on the surface of the particle, where the surface region has both large pores and small pores (See, e.g., Mangin, FIG. A), and the interior region also has both large pores and small pores (See, e.g., id, FIG. B). Mangin certainly does not explicitly or inherently disclose an embolic particle having has an interior region with pores having a mean size and a surface region with pores having a mean size, where the mean size of the pores of the interior region is greater than the mean size of the pores of the surface region,

and it would not have been obvious to modify Mangin to provide such a particle. In response to Applicant's arguments, the Examiner states:

> Regarding the Mangin reference, the particles appear to be capable of having larger pore sizes, or voids, on average, in an "interior region" of the particle as opposed to a "surface region", for example as shown in the cross-section of a particle shown in Figure B. (Office Action, page 15.)

However, Mangin's Figure B is a cross-sectional view of his particle that includes a one dimensional circumference over a two dimensional circular area representing one cross-section of the particle. As one skilled in the art would understand, an "interior region" of a particle is three dimensional and a "surface region" of a particle is two or three dimensional and therefore to obtain features of the surface and interior regions of a particle, more than one cross-sectional view of the particle is required. Accordingly, one would also understand that even though Mangin's Figure B shows that the one dimensional circumference includes pores having larger sizes than the pores in the two dimensional circular area, one cannot conclude that in a three dimensional space, Mangin's particle includes a surface region that has pores with larger mean sizes than the pores in the interior region of the particle. To strictly analyze the distribution of pore sizes in Mangin's particles, infinite numbers of cross-sectional views as shown in Mangin's Figure B are needed. In fact, nowhere does Mangin disclose or otherwise indicate that his particles have an interior region with pores having a mean size and a surface region with pores having a mean size, where the mean size of the pores of the interior region is greater than the mean size of the pores of the surface region, as recited by claims 1-7, 15, 17, 19, 21, 22, 25-31, 49-54, and 56-59.

Thus, neither Jacobsen nor Mangin, alone or in combination, discloses or renders obvious the subject matter covered by claims 1-7, 15, 17, 19, 21, 22, 25-31, 49-54, and 56-59. Accordingly, Applicants seek reconsideration and withdrawal of the rejection of these claims.

The Examiner rejected claims 1-4, 6-15, 17, 19-31, and 49-53 under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 has been amended to obviate this rejection, so the rejection should be withdrawn.

The Examiner rejected claims 1-4, 6, 7, 15, 17, 19-23, 25-31, 49-54, and 56-59 under 35 U.S.C. 103(a) as being obvious over Jacobsen et al. in view of Lanphere et al., US 2003/0185895 ("Lanphere").

Claims 1-4, 6, 7, 15, 17, 19-23, 25-31, 49-54, and 56-59 cover compositions that include particle chains having at least two connected particles and a link that connects the at least two connected particles. At least one of the at least two connected particles has an interior region with pores having a mean size and a surface region with pores having a mean size, where the mean size of the pores of the interior region is greater than the mean size of the pores of the surface region.

As noted above, Jacobsen does not disclose or render obvious the features of claims 1-4, 6, 7, 15, 17, 19-23, 25-31, 49-54, and 56-59. Lanphere does not cure the deficiencies of Jacobsen. Lanphere discloses drug delivery particles that include a reservoir region having primarily larger pores and a metering region. (See, e.g., Lanphere, Abstract.) Nowhere does Lanphere disclose or render obvious particle chains that include particles, at least one of the particles having an interior region with pores having a mean size and a surface region with pores having a mean size and the mean size of the pores of the interior region is greater than the mean size of the pores of the surface region, as recited by claims 1-4, 6, 7, 15, 17, 19-23, 25-31, 49-54, and 56-59. Even if one skilled in the art would have somehow wanted to try to combine these references, that person would not have been able to make the particle chains covered by these claims because neither Jacobsen nor Lanphere teaches how to make such particle chains. Also, Jacobsen's particles in his particle chain do not include the features of Lanphere's particles. Therefore one skilled in the art would understand that Jacobsen's method of making his particle chains would not be suitable for making particle chains that include Lanphere's particles, and accordingly, one would not know how to make particle chains that include Lanphere's particles.

Thus, neither Jacobsen nor Lanphere, alone or in combination, discloses or renders obvious the subject matter covered by claims 1-4, 6, 7, 15, 17, 19-23, 25-31, 49-54, and 56-59. Accordingly, Applicants seek reconsideration and withdrawal of the rejection of these claims.

Applicants believe the application is now in condition for allowance, which action is requested.

Please apply any charges or credits to deposit account 06-1050, referencing Attorney Docket No. 01194-459001.

Respectfully submitted,

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